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PHOTOSENSITIZED OXYGENATION OF A DIPYRRYLMETHENE*

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Although the dye-sensitized photooxygenation of monopyrroles has received increasing attention[1] beginning with the pioneering work of de Mayo and Reid[2] on pyrrole and N-ethylpyrrole and more recently with various investigations of phenyl-substituted[3] and alkyl-substituted pyrroles[1,4], there has been only one report on the photooxidation of a dipyrrole[5] and no reports on the photooxidation of dipyrrylmethenes. Our interest in the photooxidative behavior of these substances arises from our investigations on the photodestruction of biliverdin[6] and bilirubin[5,7] during jaundice phototherapy.[8] Biliverdin, which possesses a dipyrrylmethene chromophore, is produced during in vitro photooxidation of bilirubin and is thought by some workers[9] to be an important intermediate in the bilirubin breakdown. It has also been implicated as a singlet oxygen, $^1O_2$, quencher[10]. For a variety of reasons, therefore, the photooxidation behavior of a dipyrrylmethene was of interest and importance.

Our initial work was begun on the readily synthesized 3,5,3',5'-tetramethyl-4,4'-diethyldipyrrylmethene (1),[11] the hydrochloride salt of which was prepared by condensing kryptopyrrole aldehyde[12] with kryptopyrrole[13] in ether in the presence of dry HCl. The free base (1) was generated from the hydrochloride by treatment with aqueous ammonia. The rate of photooxidation of the hydrochloride of (1) in methanol was slower (50% destroyed in 12 hrs) than that of the free base (50% destroyed in 1.5 hrs). With added Rose Bengal ($^1O_2$ sensitizer) photodestruction of (1) was complete in less than 1/2 hr. A dilute (0.42 mmole %) methanolic solution of (1) containing 3.3 mg % of Rose Bengal was photolyzed[14] in a

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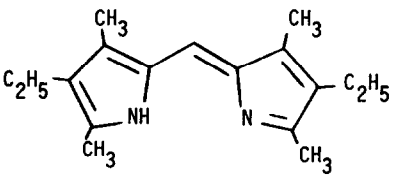
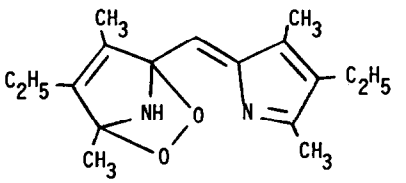
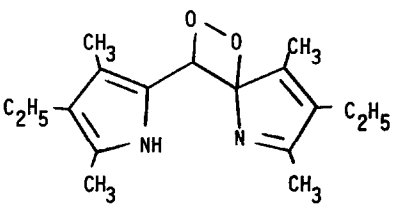
water-cooled Pyrex immersion apparatus while a slow stream (30 ml/min) of oxygen was bubbled through the reaction vessel. After a photolysis period of 50 minutes the intense longwavelength absorption maximum (445 nm) had disappeared, and the photolysis was terminated. Following evaporation of methanol *in vacuo*, the photolysate was chromotographed on silica gel (E. Merck, Darmstadt, 70-325 mesh ASTM) using a gradient elution (benzene → chloroform → ether → ethyl-acetate → methanol) technique to give a separation of four major components: 4-ethyl-5-methoxy-3,5-dimethyl-Δ^3-pyrrolin-2-one (2), 4-ethyl-5-hydroxy-3,5-dimethyl-Δ^3-pyrrolin-2-one (3), 4-ethyl-3-hydroxy-3,5-dimethyl-Δ^4-pyrrolin-2-one (4) and 4-ethyl-5-methoxymethyl-3-methyl-pyrrole-2-carboxylic acid methyl ester (5). The structures were characterized by a combination of spectroscopic methods (see Table) and also - in the case of (5) - by independent synthesis from kryptopyrrole 2-carboxylic acid methyl ester by N-bromosuccinimide monobromination at the α-methyl group followed by methanolysis.



(1)



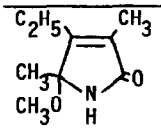
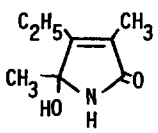
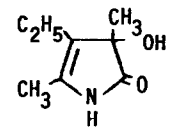
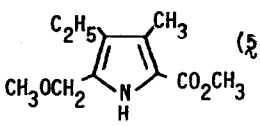
(6)



(7)

Methoxylactam (2) is visualized as arising *via* endoperoxide (6) in a manner akin to that observed for another tetrasubstituted pyrrole, 3,4-diethyl-2,5-dimethylpyrrole[15] or bilirubin.[7] Alternatively, it might arise from a secondary photooxidation on the kryptopyrrole aldehyde[16] enamating from normal cleavage[17] of dioxetane (7). Formation of (7) might be expected from the photooxidation results of bilirubin and model dipyrrylmethenones.[5] However, we cannot as yet rationalize the formation of (3), (4) and (5). Both hydroxylactams, (3) and (4) are formed during the photooxidation of kryptopyrrole.[18] It might be surmised therefore that (3) and (4) are derived from any kryptopyrrole arising *via* retrocondensation of (1). Since the relative yields of (3) and (4) from photooxidation of kryptopyrrole are more nearly 1:1[18] rather than the 2:1 seen here; kryptopyrrole cannot be the sole source of (3) and (4), if it is a precursor at all. We have also shown that (5) is a photooxidation product of kryptopyrrole 2-carboxylic acid methyl ester,[18] but other products are formed as well; hence, we cannot necessarily conclude that it is precursor to (5) in the photooxidation of (1). The mechanistic details of these reactions are currently under investigation.

Table. Physical and spectroscopic data[a] for the photooxygenation products of 3,5,3',5'-tetramethyl-4,4'-diethyldipyrrylmethene

Compound Yield (mole/mole %) M.p. (°C)	MS m/e	^{1}H-NMR ($CDCl_3$ vs. TMS, δ in ppm)	IR (KBr, cm^{-1})
 (2) 31% 84-85°	169.1105 (M^+, $C_9H_{15}NO_2$) 154 (M-CH_3) 140 (M-C_2H_5) 138 (M-OCH_3)	b 1.14 (CH_3/t) 1.48 (CH_3/s) 1.79 (CH_3/s) 2.24 (CH_2/q) 2.95 (OCH_3/s) 7.68 (NH/br. s)	1689 (ν C=O)
 (3) 22% 135-137.5°	155.0943 (M^+, $C_8H_{13}NO_2$) 140 (M-CH_3) 138 (M-OH) 126 (M-C_2H_5)	1.17 (CH_3/t) 1.51 (CH_3/s) 1.73 (CH_3/s) 2.35 (CH_2/q) 2.90-3.50 (OH/br. s) 6.83 (NH/br. s)	1670 (ν C=O)
 (4) 13% 120-122.5°	155.0941 (M^+, $C_8H_{13}NO_2$) 140 (M-CH_3) 138 (M-OH) 126 (M-C_2H_5)	1.16 (CH_3/t) 1.51 (CH_3/s) 1.80 (CH_3/s) 2.34 (CH_2/q) 7.17 (NH/br. s)	1701 (ν C=O) 1625 (ν C=C)
 (5) 8% 85-86°	211.1204 (M^+, $C_{11}H_{17}NO_3$) 196 (M-CH_3) 180 (M-OCH_3) 166 (M-CH_2OCH_3) 148 (M-CH_3OH-OCH_3) 134 (M-CH_3OH-CH_2OCH_3) 120 (M-CH_3OH-CO_2CH_3)	b 1.02 (CH_3/t 2.20 (CH_3/s) 2.37 (CH_2/q) 3.22 (OCH_3/s) 3.78 (OCH_3/s) 4.33 (OCH_2/s) 9.63 (NH/br. s)	

a Mass spectra were determined on a CEC MS 491-21 or an AEI MS-9 mass spectrometer, nuclear magnetic resonance (NMR) were run on a Varian T-60 instrument, infrared spectra were run on a Perkin-Elmer 421 spectrophotometer.

b CCl_4 solvent.

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